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FOUR NEW LABDANE DITERPENE OXIDES FROM *SIDERITIS GOMERAE**

ANTONIO G. GONZÁLEZ, BRAULIO M. FRAGA, MELCHOR G. HERNÁNDEZ, FRANCISCA LARRUGA and JAVIER G. LUIS

Department of Organic and Biochemistry, University of La Laguna, Instituto de Investigaciones Químicas, C S I C, Tenerife, Spain

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Abstract—Four new labdane diterpene oxides gomeraldehyde, 13-epigomeraldehyde, gomeric acid and 13-epigomeric acid as well as eperu-13-ene-8β,15-diol were isolated from the aerial part of *Sideritis gomerae*.

INTRODUCTION

Continuing our work on the chemical components of the genus *Sideritis* [1, 2] we have studied *S. gomerae* Bolle, an endemic of Gomera (Canary Isles). In addition to eperu-13-ene-8β,15-diol[ent-labd-13(14)-ene-8α,15-diol; **5**] we isolated the new diterpenes gomeraldehyde (ent-8,13-epoxylabdan-15-al; **1**), 13-epigomeraldehyde (ent-8,13β-epoxylabdan-15-al; **2**), gomeric acid (ent-8,13-epoxylabdan-15-oic acid; **3**) and 13-epigomeric acid (ent-8,13β-epoxylabdan-15-oic acid; **4**).†

RESULTS AND DISCUSSION

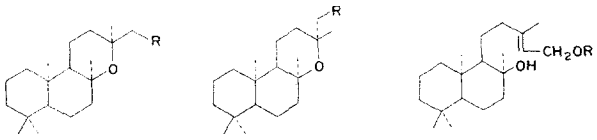
Gomeric acid (**3**) ($C_{20}H_{34}O_3$) showed IR bands indicative of an acid function (3300–2580, 1740 cm^{-1}). In the NMR spectrum characteristic signals of one CH_2COO and five methyl groups were observed. Two Me groups which appeared as a singlet at δ 1·41 must be situated on carbon atoms bearing oxygen. Treatment of (**3**) with CH_2N_2 gave the methyl ester (**7**) whose IR spectrum lacked OH absorption. Hence, the remaining oxygen must form an ether bridge. The acid was reduced with $LiAlH_4$ to the primary alcohol (**9**) (δ 3·80, 2H). On the basis of the above data (**3**) was attributed the structure of a labdane oxide possessing an acid function at C-15. A compound analogues to (**7**) was obtained by Audier *et al.* [3] on oxidizing sclareol first with CrO_3–HOAc and then with Ag_2O in alkali, followed by treatment with CH_2N_2. Direct comparison of the resulting product with our ester (**7**) revealed that they had identical mp, IR and NMR spectra but opposite optical rotations, whence they must be enantiomers Gomeric acid was therefore assigned structure (**3**)

The NMR spectrum of 13-epigomeric acid (**4**) differs from that of compound (**3**) only in the position of the C-8 and C-13 methyl and C-14 hydrogen signals, which indicates that (**4**) must be a C-13 epimer of gomeric acid. Reduction of (**4**) with $LiAlH_4$ gave the alcohol (**10**) which was identical with that obtained by hydroboration of (−)-13-epimanoyl oxide (**11**) (mp, IR, NMR).

The unstable aldehydes gomeraldehyde (**1**) and 13-epigomeraldehyde (**2**) were also isolated from *Sideritis gomerae*. They were easily oxidized by air [4] and proved to be identical (TLC, NMR) with the oxidation products of the alcohols (**9**) and (**10**) respectively, which in turn had been prepared from the corresponding acids (**3**) and (**4**) as mentioned above. The co-occurrence of C-13 epimers has been reported before [5].

* Part 26 in the series "Constituents of the Labiatae" For Part 25 see González, A. G, Bretón, J L, Fagundo, C R and Trujillo, J M (1975) *Anal Quím* (in press)

† Nomenclature is based on *The Common and Systematic Nomenclature of Cyclic Diterpenes*, 3rd revision, 1969, available from Dr J W Rowe, U S Forest Products Laboratory, Madison, Wisc 53705, U S A.



(1) R = CHO
(3) R = CO_2H
(7) R = CO_2Me
(9) R = CH_2OH

(2) R = CHO
(4) R = CO_2H
(8) R = CO_2Me
(10) R = CH_2OH
(11) R = CH_2

(5) R = H
(6) R = Ac

The fifth diterpene was identified with eperu-13-ene-8β,15-diol (**5**) by comparison with an authentic sample, previously obtained from a *Beyeria* species [6].

EXPERIMENTAL

Mp's are uncorr. Optical activities and IR spectra were taken in $CHCl_3$, NMR spectra on a 60-MHz instrument in $CDCl_3$ with TMS as internal standard. MS were measured at 70 eV (probe). Column and dry column chromatography was performed on Si gel 0·2–0·5 and 0·063–0·20 mm respectively.

Isolation of the diterpenes. The air-dried aerial part of the plant (2 kg), collected on Gomera (Canary Isles) beside the North Route at km 4 in July, was chopped and extracted several times with EtOH in a Soxhlet. The cold extract was filtered, concentrated *in vacuo* and chromatographed on a column. Petrol, petrol–EtOAc and EtOAc eluted mixtures of diterpenes and flavones which were rechromatographed on dry columns yielding the following diterpenes, in order of elution: gomeraldehyde (**1**), 13-epigomeraldehyde (**2**), gomeric acid (**3**), 13-epigomeric acid (**4**), and eperu-13-ene-8β,15-diol (**5**).

Gomeraldehyde (*ent*-8,13-*epoxylabdan*-15-*al*; (**1**), *unstable*. NMR: δ 0·76 (6H, *s*, C-18, C-19), 0·85 (3H, *s*, C-20), 1·28 and 1·32 (each 3H, *s*, C-16, C-17), 2·46 (2H, *t*, *J* 4 Hz, C-14), 9·90 (1H, *t*, *J* 4 Hz, C-15).

13-Epigomeraldehyde (*ent*-8,13β-*epoxylabdan*-15-*al*; **2**), *unstable*. NMR: δ 0·80 (6H, *s*, C-18, C-19), 0·85 (3H, *s*, C-20), 1·25 and 1·31 (each 3H, *s*, C-16, C-17), 2·33 and 2·86 (1H each, *q*, J_{AX} 4 Hz, J_{AB} 15 Hz, C-14), 9·92 (1H, *t*, *J* 4 Hz, C-15).

Gomeric acid (*ent*-8,13-*epoxylabdan*-15-*oic acid*; **3**) (4 g). Mp 113–115° (petrol), $[\alpha]_D$ −34° (*c* 0·13). (Found: C, 74·51; H, 10·42. $C_{20}H_{34}O_3$ requires: C, 74·49; H, 10·63%.) IR ν_{max} cm^{-1}: 3300–2580, 1740, 1430, 1385, 1379, 1250, 1100, 940. NMR: δ 0·84 (6H, *s*, C-18, C-19), 0·92 (3H, *s*, C-20), 1·41 (6H, *s*, C-16, C-17), 2·53 (2H, *d*, defomed AB system, C-14). MS *m/e* (%): 322 (M^+; 1), 307 (100), 289, 261 245, 191, 189, 175, 149, 137, 123. *Methyl ester* (**7**), obtained by treating (**3**) with CH_2N_2, mp 106–107° (MeOH), $[\alpha]_D$ −22° (*c* 1·46). (Found: C, 75·18; H, 10·78. $C_{21}H_{36}O_3$ requires: C, 74·95; H, 10·78%.) NMR: δ 0·82 (6H, *s*, C-18, C-19), 0·88 (3H, *s*, C-20), 1·32 and 1·36 (each 3H, *s*, C-16, C-17), 2·48 (2H, *s*, C-14), 3·70 (3H, *s*, OMe). MS *m/e* (%): 321 (M^+ − 15; 23), 306 (100), 270, 245, 137, 109.

13-Epigomeric acid (*ent*-8,13β-*epoxylabdan*-15-*oic acid*; **4**) (0·6 g). Mp 127–129° (MeOH), $[\alpha]_D$ −20° (*c* 0·60). IR ν_{max} cm^{-1}: 3320–2600, 1745, 1390, 1380, 1075, 990. NMR: δ 0·85 (6H, *s*, C-18, C-19), 0·92 (3H, *s*, C-20), 1·36 and 1·40 (each 3H, *s*, C-16, C-17), 2·55 and 2·80 (each 1H, *bs*, deformed AB system, C-14). MS *m/e* (%): 306 (M^+ − 15; 100), 288, 263, 261, 245, 230, 207, 177, 165, 163, 149, 137, 123. *Methyl ester* (**8**), obtained by treating (**4**) with CH_2N_2, would not crystallize. NMR: δ 0·78 (6H, *s*, C-18, C-19), 0·82 (3H, *s*, C-20), 1·22 (6H, *s*, C-16, C-17), 2·61 (2H, *d*, deformed AB system, C-14), 3·61 (3H, *s*, OMe).

Eperu-13-ene-8β,15-diol (*ent-labd*-13(14)-*ene*-8α,15-*diol*; **5**) (0·5 g). Mp 131–132° (petrol), $[\alpha]_D$ +0·6° (*c* 1·40) (lit. [6] mp 130·5–131·5°, $[\alpha]_D$ +0·7°). NMR: δ 0·76 (6H, *s*, C-18, C-19), 0·82 (3H, *s*, C-20), 1·12 (3H, *s*, C-17), 1·68 (3H, *s*, C-16), 4·12 (2H, *d*, *J* 8 Hz, C-15), 5·42 (1H, *t*, *J* 8 Hz, C-14). MS *m/e* (%): 290 (M^+ − 18; 7), 275, 257, 191, 177 (100), 149, 137, 123. *Acetate* (**6**), prepared as usual; NMR: δ 0·78 (6H, *s*, C-18, C-19), 0·84 (3H, *s*, C-20), 1·10 (3H, *s*, C-17), 1·69 (3H, *s*, C-16), 2·02 (3H, *s*, OAc), 4·55 (2H, *d*, *J* 8 Hz, C-15), 5·32 (1H, *t*, *J* 8 Hz, C-14).

Reduction of gomeric acid. (**3**) (140 mg) in dry Et_2O (14 ml) was refluxed with $LiAlH_4$ (170 mg) for 8 hr. Excess reagent was destroyed by adding H_2O, the mixture was washed with 10% aq. HCl and extracted with Et_2O to give the alcohol (**9**) (130 mg), mp 45–47° (MeOH), $[\alpha]_D$ −3·5° (*c* 0·60). NMR: δ 0·79 (6H, *s*, C-18, C-19), 0·83 (3H, *s*, C-20), 1·29 (6H, *s*, C-16, C-17), 3·80 (2H, *t*, C-15).

Reduction of epigomeric acid. (**4**) (50 mg) in dry Et_2O (10 ml) was reduced as described above for (**3**), yielding the alcohol (**10**) (35 mg), mp 87–89° (petrol), $[\alpha]_D$ −13° (*c* 1·50). NMR: δ 0·78 (6H, *s*, C-18, C-19), 0·84 (3H, *s*, C-20), 1·22 and 1·28 (each 3H, *s*, C-16, C-17), 3·80 (2H, *m*, C-15).

Hydroboration of (−)-13-*epimanoyl oxide* (*ent*-8,13β-*epoxy*-14-*labdene*; **11**). Through a soln of (**11**) (380 mg) in dry THF (20 ml) diborane was passed by applying a slight flow of dry N_2. Diborane was prepared by the dropwise addition of a soln of $NaBH_4$ (4 g) in diglyme (90 ml) to a stirred soln of BF_3 etherate (25 ml) in diglyme (20 ml). After completing the $NaBH_4$ addition the diborane generator was heated to boiling for 1 hr and the resulting organoborane oxidized by adding 3 N NaOH (20 ml) and 30% H_2O_2 (15 ml). The mixture was stirred for 1 hr and worked up as usual. Dry column chromatography (C_6H_6–EtOAc, 4:1) gave the alcohol (**10**) (190 mg), mp 88–90° (petrol), $[\alpha]_D$ −14° (*c* 1·70). (Found: C, 78·10; H, 11·74. $C_{20}H_{36}O_2$ requires: C, 77·87; H, 11·76%.) This compound was identical (mp, IR, NMR) with the compound obtained by reduction of (**4**).

Oxidation of (**9**) *and* (**10**). A soln of (**9**) (140 mg) in Me_2CO (10 ml) was treated dropwise with a slight excess of Jones reagent, poured into H_2O and worked up as usual, yielding the aldehyde (**1**) (90 mg) and the acid (**3**) (30 mg). Oxidation of (**10**) (160 mg) in the same way gave the aldehyde (**2**) (110 mg) and the acid (**4**) (30 mg).

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